

REVIEW ARTICLE

Ginseng and cancer

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Summary

Derived from the Greek word Panacea that means “cure for all”, Ginseng (*Panax*) has had an important place in Chinese Medicine for many of years. As the name suggests, it is believed to be a miraculous plant effective in the treatment of many health problems. It is claimed to have many effects such as sedative, hypnotic, aphrodisiac, antidepressant, diuretic, and stimulating effects, and to be effective in the treatment of certain health problems such as diabetes, Alzheimer’s disease, erectile dysfunction and infections. In addition, its effects on the prevention and treatment of cancer as well as on the reduction of cancer-related symptoms have been prioritized in recent years. However, the studies that have been done so far do not confirm these effects. Although certain favorable results have been obtained in

some studies intended for investigating its effects on acute nasopharyngitis, diabetes, Alzheimer’s disease, and erectile dysfunction, it is early to say anything conclusive. And in cancer patients, it has been shown to be effective in reducing weakness due to cancer and its treatment. On the other hand, ginseng may cause important drug interactions, although it is described as a relatively safe product. For now, it seems to be reasonable to use ginseng only for cancer-related weakness in cancer patients at this point. But this should definitely be done within the knowledge and under the control of oncologists.

Key words: alternative medicine, cancer, complementary medicine, ginseng, panax, phytotherapy

Introduction

Ginseng used for more than 2,000 years in traditional Chinese Medicine, is a plant believed to have miraculous properties and a life-extending effect, which began to make a distinguished name for itself in Western countries starting from the 18th century [1]. *Panax*, the botanical name of ginseng, is derived from the Greek word Panacea that means “cure for all” [2]. And ginseng, the English name of the plant, derives from the Chinese term rénshēn. Since the forked shape of its roots resembles the legs of a human, the Chinese word “ren” that means ‘human’ and the word “shen” that means ‘plant root’ are used [3]. Although there are 7 species of ginseng distributed in Asia and North America [1], there are basically 2 main species having medicinal properties,

on which studies are carried out. Asian (Chinese or Korean) ginseng with the Latin name ‘panax’, and American ginseng with the Latin name ‘panax quinquefolius’. Asian ginseng is also referred to as red ginseng [4,5]. Both types contain active components called ginsenosides [6]. But in traditional Chinese Medicine, Asian ginseng is defined as a ‘hot herb’ (yang), whereas American ginseng is defined as a ‘cooling herb’ (yin) due to different ginseng contents [7].

American and Asian ginsengs, claimed to be effective in the treatment of many health problems, have gained a considerable popularity, particularly in recent years. Ginseng products consumed more commonly with each passing day are produced and marketed in many forms. Ginseng

products in the forms of powder, capsule, tablet, soft gel, liquid extract, tea, and coffee are available. Moreover, certain energy drinks contain ginseng, as well [8,9]. For many years, American and Asian ginsengs have been tested for many health problems in a great number of studies such that the literature has many studies on Ginseng's effects such as sedative, hypnotic, aphrodisiac, antidepressant, diuretic, nervous system-simulating effects [10,11]. Its effects on physical performance, psychomotor performance, and HSV-2 infection have also been investigated. But ultimately, effectiveness of ginseng in any of these cases has been nothing more than a reasonable doubt [10]. There is a small number of studies indicating its effectiveness in the treatment of erectile dysfunction. However, these studies are not at a level sufficient to draw any conclusions [5]. Although the findings regarding its effects on the immune system, cognitive performance and blood glucose regulation are relatively stronger, but they have to be verified. A small-scale study that enrolled 19 individuals suggested that when taken with foods, American ginseng could be beneficial in the prevention of postprandial hypoglycaemia [12]. In another study that involved the evaluation of the long-term safety of its use as a support for the standard treatment in diabetic patients, no significant difference was observed in terms of side effects [13]. A study investigating the immune system-supporting property of American ginseng enrolled 279 people, among whom those who took 2 capsules of American ginseng a day for a period of 4 months got less acute nasopharyngitis, compared to those who did not take American ginseng [14]. In a preliminary study carried out on a small number of patients, American ginseng was observed to enhance memory performance [15]. In another study, Panax ginseng was observed to enhance the cognitive performance in Alzheimer's patients [16].

Ginseng has often been a current issue in recent years, particularly with the claims about its effects on cancer. However, there is no hard evidence that ginseng is effective in the prevention and treatment of cancer [17]. On the other hand, it has been shown to be useful in reducing the weakness associated with cancer and its treatment [18].

Ginseng in the prevention and treatment of cancer

The claims about the effects of ginseng on the prevention and treatment of cancer are basically based on laboratory studies. In a small number of

clinical studies such effects of ginseng could not be supported with hard evidence. The American Institute of Health states that there is no adequate evidence that ginseng is effective in the prevention and treatment of cancer [17].

In a laboratory study, American ginseng extract inhibited the cell growth in colorectal cancer cell lines, and this effect was found to be greater when the extract was used in conjunction with 5-fluorouracil (5-FU). In conclusion, it was stated that American ginseng would be a potential chemo-adjuvant for reducing the required dosage of 5-FU in the future [19]. In another laboratory study, American ginseng extract inhibited the proliferation in breast cancer cell lines by means of MAP kinase inhibition [20]. In another study on estrogen receptor (ER)-positive breast cancer cell cultures, American ginseng inhibited cell growth by showing a synergistic effect with methotrexate, cyclophosphamide, doxorubicin and 5-FU [21]. In another study, American ginseng extract triggered cell death in colorectal cancer cell lines, by inducing mitochondrial damage [4]. And in a study carried out on mice by using panax ginseng, it was observed to inhibit lung metastasis and angiogenesis [22]. Another study carried out on mice with implanted human ovarian cancer cells showed that administration of ginsenoside Rh₂ created a significant increase in survival [23]. In a study conducted on cervical cancer cells by Lin et al., the use of Asian ginseng (red ginseng) was found to increase the anticancer activity of paclitaxel and epirubicin [24].

In an epidemiological study conducted in 2006, women with breast cancer who used ginseng were found to have a higher quality of life and a little bit longer survival times. However, the type and doses of the ginseng were not taken into account during the study [25]. A clinical study carried out with 40 healthy participants suggested that it might have radioprotective effects on human lymphocytes [26].

Ginseng in cancer-related weakness

Weakness is one of the most common symptoms in cancer patients, which puts the patient to inconvenience and restricts physical activity. According to the statistics 59-96% of patients treated with chemotherapy and 65-100% of patients treated with radiotherapy show weakness [27] and after diagnosis, these symptoms last 5-10 years on average [28]. In cancer patients, weakness is considered to be caused by an increase in certain inflammatory cytokines and inadequate

regulation of cortisone. In some laboratory studies, anti-inflammatory and cortisol-modulating effects of ginseng were shown [29-31] and based on these reports, ginseng is thought to be effective in cancer-related weakness. In a comprehensive study presented during 2012 Annual Meeting of the American Society of Clinical Oncology (ASCO) held by Mayo Clinic Cancer Center, one of the leading oncology centers, high dose (2000 mg/day) of American ginseng was shown to be useful in cancer-related weakness [18]. In the study that enrolled 364 cancer patients from 40 different institutions and involved the trial of capsules derived from pure American ginseng roots, an improvement in cancer-related weakness representing the score of 20 points on the scale of 100 were obtained according to a standard weakness scale, after using the roots for a period of 8 weeks. In addition, it was observed to be more beneficial in those who were actively having cancer treatment compared to those whose treatment was completed. Besides, no significant difference compared to the placebo group was observed in terms of toxicity. It was also stated that particularly pure ginseng was used in the study. Ginseng products available for sale on the market show estrogen-like properties during their processing with ethanol and such products might be harmful for breast cancer patients. In this study it was concluded that when considering the limitations of familiar effective pharmacological agents, American ginseng could be tried in cases of cancer-related weakness [18]. In another study that involved a trial of panax ginseng for the treatment of cancer-related weakness, a high dose of panax ginseng (800 mg/day) was administered to 30 patients for a period of 29 days; as a result, a significant decrease was observed in weakness, with no difference in terms of side effects. When considering the fact that Panax ginseng has similar characteristics with American ginseng, it is likely to be effective in this field, but since this study is at an initial report level, it needs to be supported with new studies [32].

Potential side effects of ginseng

American ginseng is in the first category, according to the safety grading determined by the American Herbal Products Association (AHPA). In other words, it is a product generally considered to be safe when used properly [33]. In a study intended for the evaluation of dose-dependent toxicity of American ginseng, 290 people were divided into groups according to their use of ginseng, in

which 750 mg/day, 1000 mg/day, 2000 mg/day and placebo were administered. During the follow up period, no significant difference was observed between the groups in terms of toxicity [34]. Nevertheless, there are many side effect reports in the literature, especially reports on drug interactions. Certain side effects of ginseng such as nausea, diarrhea, headache, nasal bleeding, hypertension, hypotension, and breast pain have been reported [35,36]. In the literature, there are case reports showing that it can lead to acute coronary syndrome [37].

With the studies carried out, it has been ascertained that ginseng shows phytoestrogen activity by binding to estrogen receptors. For this reason, it has been emphasized that those who should abstain from estrogen should not use ginseng [38-40]. In another laboratory study, ginseng induced cell growth in breast cancer cell lines [41].

The most important concerns associated with ginseng use consist of drug interactions. Ginsenosides, the active components of ginseng, are considered responsible for such interactions. With the studies carried out, ginsenosides were shown to increase cAMP levels by inhibiting cAMP phosphodiesterase, and cause their interaction with monoamine oxidase inhibitors [42]. There is also a study on its interactions with nifedipine through CYP3A4 inhibition [43]. Similarly, it may lead to bleeding disorders by interacting with warfarin; to hepatotoxicity by interacting with imatinib; to DRESS syndrome by interacting with lamotrigine; and to the initiation of mania by interacting with antidepressants [42,44-46]. In a clinical study on 20 healthy subjects, American ginseng was shown to reduce the anti-clotting effect of warfarin and as a result, it was emphasized that physicians should question whether patients use ginseng when prescribing warfarin [47].

Conclusion

In conclusion, ginseng is a herbal product claimed to be effective in the prevention and treatment of many health problems. But most of such effects could not be revealed in the studies that have been done so far. Although studies on its effects on acute nasopharyngitis, diabetes, Alzheimer's disease, and erectile dysfunction are

promising, they are not yet adequate to be reflected in clinical procedures. And the studies intended for the prevention and treatment of cancer by means of ginseng are basically based on laboratory experiments, and they are extremely limited. Further studies are required for the clarification of ginseng's role in cancer, its appropriate dosage, side effects and drug interaction profile. Reducing cancer-related weakness is the only clear benefit of ginseng for cancer patients, which has been shown so far. It might be reasonable to consider ginseng at this point, when considering the lim-

itations of the currently available treatment options. But the issue of drug interactions requires great attention. Some of its commercial forms have been reported to be likely to cause harmful effects in breast cancer patients by showing phytoestrogenic effects. Therefore, it is extremely important for physicians to know about these interactions and follow patients closely.

Conflict of interests

The authors declare no conflict of interests.

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